Journal of Physics: Conference Series **490** (2014) 012138 doi:10.1088/1742-6596/490/1/012138

A Parallel 2D Numerical Simulation of Tumor Cells Necrosis by Local Hyperthermia

R F Reis[1], F S Loureiro[2] and M Lobosco[3]

[1,2,3]Department of Computer Science, Federal University of Juiz de Fora, Brazil

E-mail: [1]ruyfreis@gmail.com, [2]felipe.loureiro@ufjf.edu.br, [3]marcelo.lobosco@ufjf.edu.br

Abstract. Hyperthermia has been widely used in cancer treatment to destroy tumors. The main idea of the hyperthermia is to heat a specific region like a tumor so that above a threshold temperature the tumor cells are destroyed. This can be accomplished by many heat supply techniques and the use of magnetic nanoparticles that generate heat when an alternating magnetic field is applied has emerged as a promise technique. In the present paper, the Pennes bioheat transfer equation is adopted to model the thermal tumor ablation in the context of magnetic nanoparticles. Numerical simulations are carried out considering different injection sites for the nanoparticles in an attempt to achieve better hyperthermia conditions. Explicit finite difference method is employed to solve the equations. However, a large amount of computation is required for this purpose. Therefore, this work also presents an initial attempt to improve performance using OpenMP, a parallel programming API. Experimental results were quite encouraging: speedups around 35 were obtained on a 64-core machine.

1. Introduction

The tissue temperature variation caused by the magnetic nanoparticle hyperthermia process can be mathematically modeled by means of the Pennes equation [1]. Although there are other mathematical bioheat transfer models, the Pennes one is the most widely adopted in modeling due to its simplicity and good approximation [2]. Normally, heat generation in hyperthermia process is given by a quantity namely specific absorption rate (SAR) that are added to the bioheat equation as a source term. The SAR distribution and its parameters in the context of magnetic nanoparticles were determined by a previous study of temperature elevations in a rat hind limb [3].

The objective of the current study is to analyze different ways of employing injection sites inside the tumor. The tissue temperature in the hyperthermia process is written as a function of a steady-state temperature since before the heating the tumor tissue is at a higher temperature than the normal tissue. Furthermore, due to the large amount of floating point operations required to implement the numerical method, the current work also presents the speedup achieved by the parallel version of the code, developed using OpenMP[4].

2. Bioheat transfer model

The transient bioheat model used is the well-known Pennes equation given by [1]:

$$\begin{cases} \rho c\dfrac{\partial T_1(\vec{x},t)}{\partial t} = \nabla.k\nabla T_1(\vec{x},t) + \omega_b\rho_b c_b(T_a - T_1(\vec{x},t)) + Q_m(\vec{x}) + Q_r(\vec{x},t) & \text{in } \Omega, t>0 \\ \alpha T_1(\vec{x},t) + \beta\nabla T_1(\vec{x},t).\vec{n} = f(\vec{x},t) & \text{on } \Gamma, t>0 \\ T_1(\vec{x},0) = T_2(\vec{x}) & \text{in } \Omega \end{cases} \quad (1)$$

where ρ, c and k are, respectively, the density, the specific heat and thermal conductivity of the tissue; c_b, ρ_b and ω_b are, respectively, the specific heat of the blood, the density of the blood and blood perfusion rate; Q_m metabolic heat generation; T_a is the arterial blood temperature and T_1 the tissue temperature; Q_r external spatial heating.

The initial temperature, called $T_2(\vec{x})$, over the whole tissue with a tumor can be calculated from the steady-state bioheat equation considering $Q_r = 0$, that are obtained taking $\frac{\partial T(\vec{x},t)}{\partial t} = 0$.

Once the tissue temperature $T_2(\vec{x})$ is known, one can proceed with the solution of equation 1. However, to simplify the analysis of the model we use a transient equation that represents the relative temperature $\overline{T}(\vec{x},t) = T_1(\vec{x},t) - T_2(\vec{x})$ [5]. Hence, we obtain:

$$\begin{cases} \rho c\dfrac{\partial \overline{T}(\vec{x},t)}{\partial t} = \nabla.k\nabla\overline{T}(\vec{x},t) - \omega_b\rho_b c_b\overline{T}(\vec{x},t) + Q_r(\vec{x},t) & \text{in } \Omega, t>0 \\ \overline{T}(\vec{x},0) = 0 & \text{in } \Omega \end{cases} \quad (2)$$

3. Numerical scheme

The numerical method applied to solve equation 2 is the finite difference method [6]. In this way, a uniform Grid over the closed domain $\Omega \bigcup \Gamma \subseteq \mathbb{R}^2$ with coordinates $x_i = ih_x$ and $y_i = jh_y$ is constructed with h_x and h_y being the grid spacing in each direction. The discretization used in the time domain is the forward difference with a time step size h_t such that $t_n = nh_t$ while the second order central difference is employed for the spatial discratization. Hence, the discrete counterpart of equation 2 reads:

$$T^{n+1}_{i,j} = \frac{h_t}{\rho_{i,j}c_{i,j}}\left[-\frac{(q^n_{i+1/2,j} - q^n_{i-1/2,j})}{h_x} - \frac{(q^n_{i,j+1/2} - q^n_{i,j-1/2})}{h_y} - \omega_{bi,j}\rho_{bi,j}c_{bi,j}T^n_{i,j} + Q^n_{ri,j}\right] + T^n_{i,j} \quad (3)$$

where $q^n_{i+1/2,j} = -k^n_{i+1/2,j}\frac{\partial T^n_{i,j}}{\partial x} \approx -k^n_{i+1/2,j}\frac{T^n_{i+1,j} - T^n_{i,j}}{h_x}$ (all the other fluxes are approximated in a similar manner). When thermal conductivity is a smooth function, the values of $k_{i+1/2,j}$ can be computed directly at that point. However, if $k(\vec{x})$ is discontinuous as in the case of piecewise homogeneous media (e.g. tissue with tumor), the harmonic mean of the thermal conductivity expressed by $k_{i\pm1/2,j} = \frac{2k_{i,j}k_{i\pm1,j}}{k_{i,j}+k_{i\pm1,j}}$ is adopted to ensure the flux continuity.

4. Numerical simulations and parallelization strategy

All simulations performed in this study consider that above $T = 43^oC$ the cell is destroyed causing necrosis [7]. Actually, the temperature is computed in terms of $\overline{T}(\vec{x},t) = T_1(\vec{x},t) - T_2(\vec{x})$ with $T_2(\vec{x})$ being slightly higher than 37^oC due to the tumor.

In hyperthermia treatment the heat generation from the applied injection sites can be described by the so-called SAR. According to Salloum et. al [3] the SAR around the injection site due to magnetic nanoparticles can be approximated by a Gaussian distribution expressed by $SAR = A.e^{-r^2/r_0^2}$ where A represents the maximum value; r is the spatial distance from the injection site; and r_0 is how far from the injection site the heating affects the tissue. The external spatial heating Q_r accounts for the n injection sites which is represented by $Qr(\vec{x},t) = \sum_{i=1}^{n} A_i.e^{-r(\vec{x})_i^2/r_{0,i}^2}$

In the model analyzed here, we consider a square domain with length $0.1m$ and a square tumor with length $0.02m$ located at the center of the domain. The thermal conductivity considered for normal tissue and tumor are $k = 0.5W/m^oC$ and $k = 0.55W/m^oC$, respectively; the blood density $\rho_b = 1000.0Kg/m^3$; the blood specific heat $c_b = 4200.0J/Kg^oC$; the blood perfusion rate for normal tissue and tumor are, respectively, $\omega_b = 5.10^{-4}s^{-1}$ and $\omega_b = 1.25.10^{-3}s^{-1}$.This study was divided into 2 cases, the first assumes a single injection site and the second one 4 injection sites. At both cases we consider a hyperthermia with 50 min of duration. In the first case the Gaussian distribution SAR parameters are assumed to be $A = 1.3.10^6W$ and $r_0 = 3.1.10^{-3}m$[7] while in the second case $A = 0.325.10^6W$ and $r_0 = 3.1.10^{-3}m$ for each injection site, in other words, each injection site has a quarter power of the first case.

Figure 1 depicts the temperature distribution in both cases, and Figure 2 the temperature time histories at two distinct points, one located in the health tissue at $(x = 0.030, y = 0.050)$ and another one inside the tumor at $(x = 0.045, y = 0.050)$.

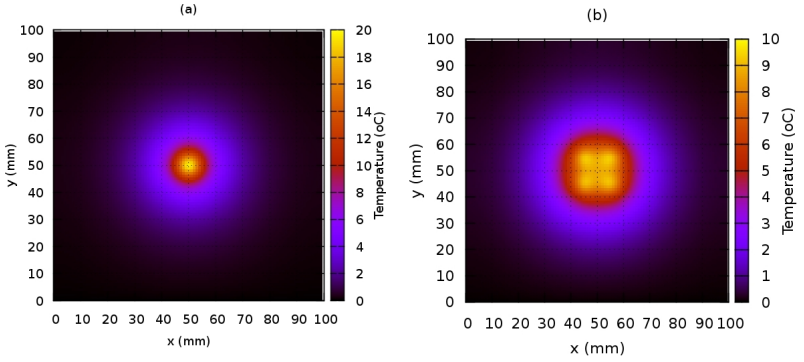

Figure 1. Temperature contour plot at $t = 50$min: (a) one injection site; and (b) four injection sites

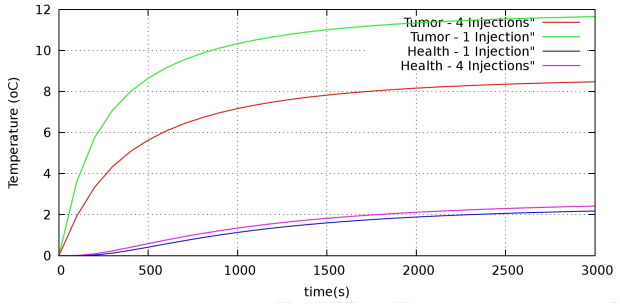

Figure 2. Temperature time-histories inside and outside the tumor in both cases

It is worth mentioning the effectiveness of the tumor necrosis at both cases. However, in the former we get 78.75% of tumor necrosis and 0.125% of health tissue necrosis, while in the latter we get 91.75% of tumor necrosis and 0.260% of health tissue necrosis. The point is that with four injection sites more tumor cells are affected compared to one injection site which means that the temperature is more distributed at the latter case.

However, this sequential version of the code takes almost 10 hours to execute a simulation. In order to reduce this huge execution time, a parallel version of the code was implemented using OpenMP[4]. Due to dependencies among distinct time-steps, only the computation of the

spatial discretization was implemented in parallel. Supposing that the domain is discretized into $N_x \times N_y$ grid points, each thread is responsible for processing $(N_x \times N_y)/n$ points, where n is the number of threads. Although the loop that implements the spatial computation is nested into the temporal loop, threads are created only once, before the temporal loop, and then associated statically with the spatial data it must compute, so thread creation overhead is paid only once.

Our experiments were performed on a SMP Linux (3.9.2-200) computer, consisting of 4 AMD Opteron 6272 CPU and 128 GB of RAM. Each CPU has 16 cores, so a total of 64 cores are available. It is worthwhile to note that in this CPU two cores share a single FPU. This architectural characteristic hurts performance. In particular, depending on the way threads are scheduled, two distinct threads can dispute the same FPU, even when the number of threads are below to the total number of FPUs available. The speedup presented in Figure 3 were obtained using the average value from three executions whose standard deviation was below to 0.4957. As one can observe, the results are quite encouraging: speedups up to 35 were achieved, which means that the execution time drops from 10 hours to about 16 minutes.

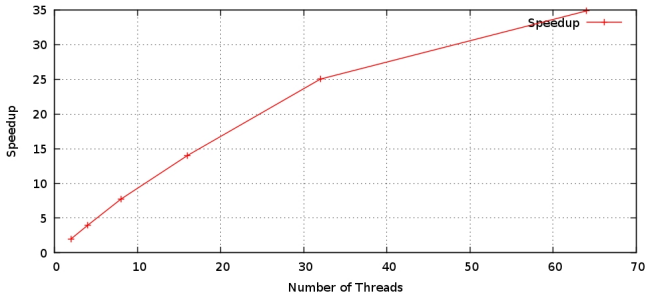

Figure 3. Speedups on a 64-core computer

Conclusions

A numerical simulation of tumor cells necrosis using hyperthermia by applying magnetic nanoparticles has been presented. It has been observed that the number of injection sites and their locations inside the tumor play an important role to achieve the desired temperature distribution (recall that hyperthermia normally involves heating tissue above $T = 43^oC$). Moreover, speedups up to 35 were achieved. As a future work, we plan to handle more complex models in 3D using for this purpose GPUs[8].

Acknowledgements

The financial support by CNPq, CAPES, UFJF and FAPEMIG is greatly acknowledged.

References

[1] Pennes H H 1948 *Journal of Applied Phisiology* **1** 93–122
[2] Minkowycz W J and Sparrow E M 2009 *Advances in Numerical Heat Transfer* 1st ed vol 3 (CRC Press)
[3] Salloum M, Ma R and Zhu L 2008 *International Journal of Hyperthermia* **24** 589–601
[4] Chandra R, Dagum L, Kohr D, McDonald D M J and Menon R 2001 *Parallel Programming in OpenMP* (Morgan Kaufmann Publishers)
[5] Liu J and Xu L 1999 *Biomedical Engineering, IEEE Transactions on* **46** 1037–1043
[6] RJ L 2007 *Finite Difference Methods for Ordinary and Partial Differential Equations, Steady State and Time Dependent Problems* 1st ed (SIAMl)
[7] Salloum M, Ma R and Zhu L 2009 *International Journal of Hyperthermia* **25** 309–321 pMID: 19670098
[8] Sanders J and Kandrot E 2010 *CUDA by Example* 1st ed (Addison-Wesley Professional)